

Package leaflet: Information for the user

Piperacillin/Tazobactam 2 g/0.25 g Powder for solution for infusion **Piperacillin/Tazobactam 4 g/0.5 g Powder for solution for infusion**

piperacillin/tazobactam

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Piperacillin/Tazobactam is and what it is used for
2. What you need to know before you are given Piperacillin/Tazobactam
3. How Piperacillin/Tazobactam is given
4. Possible side effects
5. How to store Piperacillin/Tazobactam
6. Contents of the pack and other information

1. What Piperacillin/Tazobactam is and what it is used for

Piperacillin belongs to the group of medicines known as “broad spectrum penicillin antibiotics”. It can kill many kinds of bacteria. Tazobactam can prevent some resistant bacteria from surviving the effects of piperacillin. This means that when piperacillin and tazobactam are given together, more types of bacteria are killed.

Piperacillin/Tazobactam is used in adults and adolescents to treat bacterial infections, such as those affecting the lower respiratory tract (lungs), urinary tract (kidneys and bladder), abdomen, skin or blood. Piperacillin/Tazobactam may be used to treat bacterial infections in patients with low white blood cell counts (reduced resistance to infections).

Piperacillin/Tazobactam is used in children aged 2-12 years to treat infections of the abdomen such as appendicitis, peritonitis (infection of the fluid and lining of the abdominal organs), and gallbladder (biliary) infections. Piperacillin/Tazobactam may be used to treat bacterial infections in patients with low white blood cell counts (reduced resistance to infections).

In certain serious infections, your doctor may consider using Piperacillin/Tazobactam in combination with other antibiotics.

2. What you need to know before you are given Piperacillin/Tazobactam

Do not use Piperacillin/Tazobactam

- if you are allergic to piperacillin or tazobactam.
- if you are allergic to antibiotics known as penicillins, cephalosporins or other beta-lactamase inhibitors, as you may be allergic to Piperacillin/Tazobactam.

Warnings and precautions

Talk to your doctor or nurse before you are given Piperacillin/Tazobactam

- if you have allergies. If you have several allergies, make sure you tell your doctor or other healthcare professional before receiving this product.
- if you are suffering from diarrhoea before, or if you develop diarrhoea during or after your treatment. In this case, make sure you tell your doctor or other healthcare professional immediately. Do not take any medicine for the diarrhoea without first checking with your doctor.
- if you have low levels of potassium in your blood. Your doctor may want to check your kidneys before you take this medicine, and may perform regular blood tests during treatment.
- if you have kidney or liver problems, or are receiving haemodialysis. Your doctor may want to check your kidneys before you take this medicine, and may perform regular blood tests during treatment.
- if you are taking certain medicines (called anticoagulants) to avoid an excess of blood clotting (see also **Using other medicines** in this leaflet) or any unexpected bleeding occurs during the treatment. In this case, you should inform your doctor or other healthcare professional immediately.
- if you develop convulsions during the treatment. In this case, you should inform your doctor or other healthcare professional.
- if you think you developed a new or worsening infection. In this case, you should inform your doctor or other healthcare professionals.

Haemophagocytic lymphohistiocytosis

There have been reports about a disease in which the immune system makes too many of otherwise normal white blood cells called histiocytes and lymphocytes, resulting in inflammation (haemophagocytic lymphohistiocytosis). This condition may be life-threatening if not diagnosed and treated early. If you experience multiple symptoms such as fever, swollen glands, feeling weak, feeling lightheaded, shortness of breath, bruising, or skin rash, contact your doctor immediately.

Children

Piperacillin / tazobactam is not recommended for use in children below the age of 2 years due to insufficient data on safety and effectiveness.

Other medicines and Piperacillin/Tazobactam

Tell your doctor if you are using, have recently used or might use any other medicines. Some medicines may interact with piperacillin and tazobactam.

These include:

- medicine for gout (probenecid). This can increase the time it takes for piperacillin and tazobactam to leave your body.
- medicines to thin your blood or to treat blood clots (e.g. heparin, warfarin or aspirin).
- medicines used to relax your muscles during surgery. Tell your doctor if you are going to have a general anaesthetic.
- methotrexate (medicine used to treat cancer, arthritis or psoriasis). Piperacillin and tazobactam can increase the time it takes for methotrexate to leave your body.
- medicines that reduce the level of potassium in your blood (e.g. tablets enhancing urination or some medicines for cancer).
- medicines containing the other antibiotics tobramycin, gentamycin or vancomycin. Tell your doctor if you have kidney problems.

Effect on laboratory tests

Tell the doctor or laboratory staff that you are taking Piperacillin/Tazobactam if you have to provide a blood or urine sample.

Pregnancy and breast-feeding

Piperacillin and tazobactam can pass to a baby in the womb or through breast milk. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor before getting this product. Your doctor will decide if Piperacillin/Tazobactam is right for you.

Driving and using machines

The use of Piperacillin/Tazobactam is not expected to affect the ability to drive or use machines.

Piperacillin/Tazobactam contains sodium

Piperacillin/Tazobactam 2g /0.25g: This medicine contains 108 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 5.4 % of the recommended maximum daily dietary intake of sodium for an adult.

Piperacillin/Tazobactam 4g /0.5g: This medicine contains 216 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 10.8 % of the recommended maximum daily dietary intake of sodium for an adult.

The maximum recommended daily dose of this medicine contains 864 mg sodium (found in table salt). This is equivalent to 43.2 % of the recommended maximum daily dietary intake of sodium for an adult.

Talk to your doctor or pharmacist if you need Piperacillin/Tazobactam on a daily basis for a prolonged period, especially if you have been advised to follow a low salt (sodium) diet.

3. How Piperacillin/Tazobactam is given

Your doctor or nurse will give you this medicine through an infusion (a drip for 30 minutes) into one of your veins.

The dose of medicine given to you depends on what you are being treated for, your age, and whether or not you have kidney problems.

You will be given Piperacillin/Tazobactam until the signs of infection have gone completely (5 to 14 days).

Adults and adolescents aged 12 years or older

The recommended dose is 4g/0.5 g piperacillin/tazobactam given every 6-8 hours, which is given into one of your veins (directly into the blood stream).

Children aged 2 to 12 years

The recommended dose for children with abdominal **infections** is 100 mg / 12.5 mg / kg of body weight of piperacillin/tazobactam given every 8 hours into one of your veins (directly into the blood stream). The usual dose for children with low white blood cell counts is 80 mg / 10 mg / kg of body weight of piperacillin / tazobactam given every 6 hours into one of your veins (directly into the blood stream).

Your doctor will calculate the dose depending on your child's weight but each individual dose will not exceed 4 g / 0.5 g of piperacillin/tazobactam.

Patients with kidney problems

Your doctor may need to reduce the dose of Piperacillin/Tazobactam or how often you are given it. Your doctor may also want to test your blood to make sure that your treatment is at the right dose, especially if you have to take this medicine for a long time.

If you are given more Piperacillin/Tazobactam than you should

As you will receive Piperacillin/Tazobactam from a doctor or other healthcare professional, you are unlikely to be given the wrong dose. However, if you experience side effects, such as convulsions, or think you have been given too much, tell your doctor immediately.

If you miss a dose Piperacillin/Tazobactam

If you think you have not been given a dose of Piperacillin/Tazobactam, tell your doctor or other healthcare professional immediately.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

See a doctor immediately if you experience any of these potentially serious side effects of Piperacillin/Tazobactam:

The serious side effects (with frequency in brackets) of Piperacillin/Tazobactam are:

- serious skin rashes [Stevens-Johnson syndrome, dermatitis bullous (Not known), dermatitis exfoliative (Not known), toxic epidermal necrolysis (Rare)] appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs include ulcers in the mouth, throat, nose, extremities, genitals and conjunctivitis (red and swollen eyes). The rash may progress to widespread blistering or peeling of the skin and potentially may be life-threatening
- severe potentially fatal allergic condition [drug reaction with eosinophilia and systemic symptoms (Not known)] that can involve the skin and most importantly other organs under the skin such as the kidney and the liver
- a skin condition [acute generalised exanthematous pustulosis (Not known)] accompanied by fever, which consists of numerous tiny fluid filled blisters contained within large areas of swollen and reddened skin
- swelling of the face, lips, tongue or other parts of the body (Not known)
- shortness of breath, wheezing or trouble breathing (Not known)
- severe rash or hives (Uncommon), itching or rash on the skin (Common)
- yellowing of the eyes or skin (Not known)
- damage to blood cells like decrease in platelets (thrombocytopenia), decrease of red blood cells (anaemia, haemolytic anaemia) or blood pigment / haemoglobin (Common), severe decrease in white blood cells [neutropenia, leucopenia (Uncommon)]. Signs can include being breathless when you do not expect it, red or brown urine, nosebleeds or small spot bruising.
- serious infection of the colon including severe or persistent diarrhoea accompanied by a fever or weakness (Rare)

Other side effects:

If any of **the following** side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or other healthcare professional.

Very common side effects (may affect more than 1 in 10 people):

- diarrhoea

Common side effects (*may affect up to 1 in 10 people*):

- yeast infection
- abnormal lab test (positive direct Coombs), prolonged blood clotting time (activated partial thromboplastin time prolonged)
- decrease in blood protein
- headache, sleeplessness
- abdominal pain, vomiting, nausea, constipation, upset stomach
- increase in blood liver enzymes
- abnormal kidney blood tests
- fever, injection site reaction

Uncommon side effects (*may affect up to 1 in 100 people*):

- prolonged blood clotting time (prothrombin time prolonged)
- decreased blood potassium, decreased blood sugar
- low blood pressure, inflammation of the veins (felt as tenderness or redness in the affected area), reddening of skin
- increase of a blood pigment breakdown product (bilirubin)
- skin reactions with redness, formation of skin lesions, nettle rash

- joint and muscle pain
- chills

Rare side effects (*may affect up to 1 in 1,000 people*):

- inflammation of the mucous lining of the mouth

Not known side effects (*cannot be estimated from the available data*):

- bleeding time prolonged, increase of platelets (thrombocytosis), increase of a specific type of white blood cells (eosinophilia)
- allergic reaction and severe allergic reaction
- inflammation of the liver
- poor kidney functions and kidney problems
- a form of lung disease where eosinophils (a form of white blood cell) appear in the lung in increased numbers

Piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Piperacillin/Tazobactam

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label and carton after “EXP”. The expiry date refers to the last day of that month.

Powder:

Do not store above 25 °C.

Reconstituted/Diluted Product:

For storage conditions for the reconstituted/Diluted product see “The following information is intended for healthcare professionals only:” at the end of the package leaflet.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment

6. Contents of the pack and other information

What Piperacillin/Tazobactam contains

Each vial contains 2 g piperacillin (as sodium salt) and 0.25 g tazobactam (as sodium salt).

Each vial contains 4 g piperacillin (as sodium salt) and 0.5 g tazobactam (as sodium salt).

There are no other ingredients.

What Piperacillin/Tazobactam looks like and contents of the pack

Piperacillin/Tazobactam is a white to off-white powder for solution for infusion packaged in glass vials, packed in cartons containing 1, 5, 10 or 12 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Stragen UK Ltd
Castle Court
41 London Road
Surrey
RH2 9RJ

Manufacturer

Mitim S.r.l.
Via Cacciamali 34/38
25125 Brescia
Italy

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The following information is intended for healthcare professionals only:

Piperacillin/Tazobactam Powder for solution for or infusion

This is an extract from the Summary of Product Characteristics to assist in the administration of Piperacillin/Tazobactam. When determining appropriateness of use in a particular patient, the prescriber should be familiar with the SmPC.

Instructions for use

Piperacillin/Tazobactam will be given by intravenous infusion (a drip for 30 minutes).

Incompatibilities with diluents and other medicinal products

- Lactated Ringer's solution is not compatible with Piperacillin/Tazobactam.
- When used concurrently with another antibiotic (e.g. aminoglycosides), Piperacillin/Tazobactam must be administered separately. Mixing with an aminoglycoside in vitro can cause inactivation of the aminoglycoside.
- Piperacillin/Tazobactam should not be mixed with other drugs in a syringe or infusion bottle since compatibility has not been established.
- Piperacillin/Tazobactam should be administered through an infusion set separately from any other drugs unless compatibility is proven.
- Due to chemical instability, Piperacillin/Tazobactam should not be used in solutions that contain sodium bicarbonate.
- Piperacillin/Tazobactam should not be added to blood products or albumin hydrolysates.

Reconstitution directions

The reconstitution and dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discolouration prior to administration. The solution should only be used if the solution is clear and free from particles.

Intravenous use

Reconstitute each vial with the volume of solvent shown in the table below, using one of the compatible solvents for reconstitution. To reconstitute, tap lightly the vial to loosen powder from the bottom and sides. Wet all of the internal surface of the vial with solvent whilst shaking continuously. Shake until the powder is dissolved, reconstitution generally occurs within 5 to 10 minutes (for details on handling, please see below).

Content of the vial	Volume of solvent* to be added to vial
2 g / 0.25 g (2 g piperacillin and 0.25 g tazobactam)	10 ml

4 g / 0.5 g (4 g piperacillin and 0.5 g tazobactam)	20 ml
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*** Compatible solvents for reconstitution:**

- 0.9% (9 mg/ml) sodium chloride solution for injection
- Water for injections⁽¹⁾

⁽¹⁾ Maximum recommended volume of water for injection per dose is 50 ml.

The reconstituted solutions should be withdrawn from the vial by syringe. When reconstituted as directed, the vial contents withdrawn by syringe will provide the labelled amount of piperacillin and tazobactam.

The reconstituted solutions may be further diluted to the desired volume (e.g. 50 ml to 150 ml) with one of the following compatible solvents:

- Water for injections⁽¹⁾
- 0.9% (9 mg/ml) sodium chloride solution for injection
- Dextrose 5%

For single use only. Discard any unused solution.

Any unused product or waste material should be disposed of in accordance with local requirements.

SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25° C.

After reconstitution, chemical and physical in-use stability has been demonstrated for 24 hours when stored in a refrigerator at 2-8°C.

After reconstitution and dilution, chemical and physical in-use stability has been demonstrated for 48 hours when stored in a refrigerator at 2-8°C.

From a microbiological point of view, once opened, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.